Claims

1. An isolated nucleic acid molecule encoding a human neurotrophic growth factor designated enovin and having the amino acid sequence illustrated in Figure 1, or encoding a functional equivalent, derivative or bioprecursor of said growth factor.

2. A nucleic acid molecule according to claim 1 which is a DNA molecule.

3. A nucleic acid molecule according to claim 1 which is a cDNA molecule.

4. A nucleic acid molecule according to claim 3 having the nucleic acid sequence from positions 81 to 419 illustrated in Figure 1.

5. A nucleic acid molecule according to claim 1 having the nucleic acid sequence illustrated in any of Figures 1 or 21 or a molecule capable of hybridising thereto under conditions of high stringency.

6. An antisense molecule capable of hybridising to the nucleic acid molecule defined in claim 1 under high stringency conditions.

7. An isolated human neurotrophic growth factor encoded by a nucleic acid molecule as defined in claim 1.

8. A growth factor according to claim 7 comprising the amino acid sequence from position 27 to

139 of the amino acid sequence illustrated in Figure 1, or a functional equivalent, derivative or bioprecursor of said growth factor.

9. A growth factor according to claim 8 comprising the amino acid sequence illustrated in Figure 1 or a functional equivalent, derivative or bioprecursor of said growth factor.

10. An expression vector comprising a DNA molecule according to claim 2.

11. An expression vector comprising an antisense molecule according to claim 6.

12. An expression vector according to claim 10 or 11 comprising a further nucleic acid sequence encoding a reporter molecule.

13. A host cell transformed or transfected with the vector according to claim 10 or ~~11~~.

14. A host cell according to claim 13 which cell is a eukaryotic or bacterial cell.

15. A transgenic cell, tissue or organism comprising a transgene capable of expressing a human neurotrophic factor enovin according to claim 7.

16. A transgenic cell, tissue or organism according to claim 15, wherein said transgene comprises a vector according to claim 10.

17. A neurotrophic growth factor or a functional equivalent, derivative or bioprecursor thereof, expressed by a cell according to claim 13.

18. A neurotrophic growth factor or a functional equivalent, derivative or bioprecursor thereof, expressed by a transgenic cell, tissue or organism according to claim 15.

19. A method for treating or preventing neural disorders in a subject said method comprising administering to said subject an amount of a nucleic acid molecule according to claim 1 in sufficient concentration to reduce the symptoms of said neural disorders.

20. A method according to claim 19 wherein said neural disorder is selected from any of the group consisting of Parkinson's disease, Alzheimer's disease, neuronal disorders associated with expanded polyglutamine sequences such as Huntingdons disease, peripheral neuropathy, acute brain injury, nervous system tumours, multiple sclerosis, amyotrophic lateral sclerosis, peripheral nerve trauma, injury exposure to neurotoxins, multiple endocrine neoplasia, familial Hirschsprung disease, Prion associated diseases, Creutzfeld - Jacob disease, cancer or stroke.

21. A method for treating or preventing neural disorders said method comprising administering to a subject an amount of a human neurotrophic growth factor according to claim 7 in sufficient

concentration to reduce or prevent the symptoms of said neural disorders.

22. A method according to claim 21 wherein said neural disorder is selected from any of the group consisting of Parkinson's disease, Alzheimer's disease, neuronal disorders associated with expanded polyglutamine sequences, such as, Huntingdon's disease; peripheral neuropathy, acute brain injury, nervous system tumours, multiple sclerosis, amyotrophic lateral sclerosis, peripheral nerve trauma or injury or exposure to neurotoxins, multiple endocrine neoplasia familial Hirschsprung disease, Prion associated diseases, Creutzfeld - Jacob disease, cancer or stroke.

23. A pharmaceutical composition comprising a nucleic acid molecule according to claim 1 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

24. A pharmaceutical composition comprising a growth factor according to claim 7, together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

25. A method of preventing or treating neural disorders in a subject said method comprising implanting in said subject cells that express a human neurotrophic growth factor as defined in claims 7.

26. A method according to claim 25 which neural disorders are selected from the group of any of

Parkinson's disease, Alzheimer's disease, neuronal disorders associated with expanded polyglutamine sequences, such as, Huntingdon's disease, peripheral neuropathy, acute brain injury, nervous system tumours, multiple sclerosis, amyotrophic lateral sclerosis, peripheral nerve trauma or injury exposure to neurotoxins, multiple endocrine neoplasia and familial Hirschsprung disease, Prion associated diseases, Creutzfeld - Jacob disease, cancer or stroke.

27. An antibody capable of binding to a growth factor according to claim 7 or an epitope thereof.

28. A method of detecting for the presence of a growth factor in a sample which method comprises reacting an antibody according to claim 27 with said sample and detecting for any binding of said antibody with said growth factor.

29. A method according to claim 28 wherein said antibody is conjugated to a reporter molecule.

30. A kit or device for detecting for the presence of a neurotrophic growth factor in a sample comprising an antibody according to claim 27 and means for reacting said antibody and said sample.

31. A method of treating or preventing a disorder mediated by expression of enovin comprising administering to a subject an amount of an antisense molecule according to claim 6 in sufficient concentration to alleviate or prevent the symptoms of

said disorder.

32. A method of identifying an agonist or antagonist of a human neurotrophic growth factor said method comprising contacting a cell tissue or organism expressing a receptor of said growth factor and cRET with a candidate compound in the presence of said growth factor and comparing the levels of RET activation in said cell, tissue or organism with a control which has not been contacted with said candidate compound.

33. A method according to claim 32 wherein said growth factor is enovin.

34. A compound identified as an agonist or an antagonist of a growth factor according to the method of claim 32.

35. A compound identified as an agonist or an antagonist of enovin according to the method of claim 33.

36. A method of treating or preventing disorders mediated by human neurotrophic growth factor enovin which method comprises administering to a subject an amount of a compound identified as an antagonist of enovin according to claim 35 in sufficient concentration to reduce or prevent the symptoms of said disorder.

37. A method of treating or preventing a disorder mediated by inactivation of human neurotrophic growth

factor enovin, which method comprises administering to an individual an amount of a compound identified as an agonist of enovin according to claim 35 in a sufficient concentration to reduce or prevent the symptoms of said disorders.

38. A pharmaceutical composition comprising a compound according to claim 34 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

39. A method for making a pharmaceutical formulation for the treatment of diseases associated with human neurotrophic growth factor enovin, said method comprising, selecting a candidate compound identified as an agonist or antagonist of enovin according to claim 35, manufacturing bulk quantities of said compound and formulating the compound manufactured in a pharmaceutically acceptable carrier.

40. A pharmaceutical composition comprising an antibody according to claim 27 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

41. An isolated human neurotrophic growth factor comprising a polypeptide which has at least 85% sequence identity with the amino acid sequence illustrated in any one of Figures 1, 21, 23 or 24.

42. Plasmid EVNmat/pRSETB deposited under LMBP Accession No. LMBP 3931.

43. An isolated nucleic acid molecule according to claim 1 having a nucleic acid sequence corresponding to the sequence of the splice variants designated from position 5'-1 to 3'-1 or 3'-2 or from 5'-1 or 5'-2 to 3'-2 or 3'-3 of the sequence illustrated in Figure 21.

44. A neurotrophic growth factor according to claim 7 comprising the amino acid sequence illustrated in Figure 23 or 24.

45. A method of identifying agonists or antagonists of a neurotrophic growth factor said method comprising contacting a cell tissue or organism expressing a receptor of said growth factor and cRET with a candidate compound in the presence of an appropriate neurotrophic growth factor, monitoring the level of activation of a signalling kinase in the signal transduction pathway of which said receptor is a component following addition of an antibody specific for said signal kinase conjugated to a reporter molecule compared to a similar cell tissue or organism which has not been contacted with said compound.

46. A method according to claim 45 wherein said neurotrophic growth factor is enovin.

47. A method according to claim 45 wherein said cell tissue or organism is an NIH 3T3 cell.

48. A method according to claim 45 wherein said receptor is any of GFRα1, GFRα2, GFRα3 or GFRα4.

49. A method according to claim 43 wherein said antibody is specific for any of p42/p44 MAP kinase, PKB kinase, c-jun, CREB, JNK/SAPIC kinase.

50. A compound identified as an agonist or an antagonist of a neurotrophic growth factor according to the method of claim 45.

51. A compound identified as an agonist or an antagonist of enovin according to the method of claim 46.

52. A method of treating a gastrointestinal disorder mediated by hampered or impaired gastrointestinal transit, said method comprising administering to a subject an amount of an agonist according to any of claims 35, 50 or 51, or a nucleic acid molecule according to claim 1, or a growth factor according to claim 7 in sufficient concentration to reduce or prevent the symptoms of said disorder.

53. A method according to claim 52 wherein said disorder is selected from the group consisting of any of gastrooesophageal reflux, dyspepsia, gastroparesis, post operative ileus and intestinal pseudo-obstruction decreased peristalsis of the small or large intestine and/or delayed gastric emptying, constipation, intestinal atony, post-operative intestinal atony, irritable bowel syndrome (IBS), drug induced delayed transit, emesis and cytotoxic drug and radiation induced emesis.

54. A method of treating a gastrointestinal

disorder mediated by increased peristaltic intestinal movement, comprising administering to a subject a compound selected from the group consisting of a compound identified as an antagonist according to any of claims 35, 50 or 51, a nucleic acid molecule according to claim 1 and a growth factor according to claim 7 in sufficient concentration to reduce or prevent the symptoms of said disorder.

55. A method according to claim 54 wherein said disorder is selected from the group consisting of any of diarrhea, including secretory diarrhea, bacterial induced diarrhoea, choleric diarrhoea, travellers diarrhoea, and psychogenic diarrhoea, Crohns disease, spastic colon, irritable bowel syndrome (IBS) diarrhoeapredominant irritable bowel syndrome, bowel hypersensitivity and the reduction of pain associated with gastrointestinal hypersensitivity.

56. A method of treating a neural disorder mediated by over or underexpression or activity of enovin, which method comprises administering to a subject an amount of a compound according to claim 51 in a sufficient amount to alleviate or prevent the symptoms of said disorder.

57. A method according to claim 56 wherein said disorder comprises any of the group consisting of Parkinson's disease, Alzheimer's disease, neuronal disorders associated with expanded polyglutamine sequences such as Huntingdons disease, peripheral neuropathy, acute brain injury, nervous system tumours, multiple sclerosis, amyotrophic lateral

sclerosis, peripheral nerve trauma, injury exposure to neurotoxins, multiple endocrine neoplasia, familial Hirschsprung disease, Prion associated diseases, Creutzfeld - Jacob disease or stroke.

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